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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/781,384	02/18/2004	David Spencer	HO-P02165US1	2112

26271 7590 06/27/2007
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EXAMINER	
LI, QIAN JANICE	
ART UNIT	**PAPER NUMBER**
1633	

MAIL DATE	DELIVERY MODE
06/27/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/781,384	SPENCER ET AL.	
	Examiner	Art Unit	
	Q. Janice Li, M.D.	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 May 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *25,27-33,41,43,44 and 46-95* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *25,27-33,41,43,44 and 46-95* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 5/7/07 has been entered.

The amendment and response filed 5/7/07 are acknowledged. Claims 26, 34-40, 42, 45 have been canceled; Claims 54-95 are newly submitted. Claims 25, 27-33, 41, 43, 44, 46-95 are pending and under current examination.

Unless otherwise indicated, previous rejections that have been rendered moot in view of the amendment to pending claims will not be reiterated.

Claim Objections

Claim 41 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Claim 41 recites the APC is transduced with the nucleic acid ex vivo, and depends from claim 25, which recites transducing an APC in vitro or ex vivo. It is well-accepted in the art that both phrases

have the meaning of "in an artificial environment outside the living organism". Further, the specification acknowledges, "One of skill in the art is aware that ex vivo and in vitro can be used interchangeably" (Specification, paragraph 0050), and thus claim 41 fails to further limit claim 25.

Claim 41 is objected to under 37 CFR 1.75 as being a substantial duplicate of claim 25. When two claims in an application are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 25, 27-33, 41, 43, 44, 46-53, 56-71, 74-91, 94, 95 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The methodology for determining adequacy of Written Description to convey that applicant was in possession of the claimed invention includes determining whether the application describes an actual reduction to practice, determining whether the invention is complete as evidenced by drawings, or determining whether the invention has been set forth in terms of distinguishing identifying characteristics as evidenced by other descriptions of the invention that are sufficiently detailed to show that applicant was in possession of the claimed invention (*Guidelines for Examination of Patent Applications under 35 U.S.C. § 112, p 1 "Written Description" Requirement;* Federal Register/ Vol 66. No. 4, Friday, January 5, 2001; II Methodology for Determining Adequacy of Written Description (3.)).

The amended claims embrace a chimeric protein coding sequence, where the chimeric protein comprises a ligand-binding region that can bind to a FK506 and/or FK506 analog molecule. Given the broadest reasonable interpretation, the phrase encompasses a genus of ligand-binding regions capable of binding to a FK506 molecule or an analog thereof. However, the only such ligand-binding region taught in the specification is the FK506-binding region (e.g. FKBP12), the specification fails to teach any other ligand-binding region that is capable of binding to FK506 and its analogs.

In analyzing whether the written description requirement is met for the claimed subject matter i.e. a genus of ligand-binding regions that perform a particular function, one needs to disclose a representative number of species by their structures, and other relevant identifying characteristics. Considering the numbers and variety of ligand-

binding regions known or unknown in the art that are capable of binding FK506 and its analogs, the one exemplary embodiment is not the representative species of the genus.

An adequate written description for a genus requires more than a mere statement that it is part of the invention; what is required is a description of the structure of the ligand-binding regions. With respect to the method claims, adequate description of the methods first requires an adequate description of the materials, i.e. specific ligand-binding regions, which provide the means for practicing the invention. The court has made it very clear "CONCEPTION OF CHEMICAL COMPOUND REQUIRES THAT INVENTOR BE ABLE TO DEFINE COMPOUND SO AS TO DISTINGUISH IT FROM OTHER MATERIALS, AND TO DESCRIBE HOW TO OBTAIN IT, RATHER THAN SIMPLY DEFINING IT SOLELY BY ITS PRINCIPAL BIOLOGICAL ACTIVITY". *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016 (Fed. Cir. 1991).

The Revised Interim Guidelines state "THE CLAIMED INVENTION AS A WHOLE MAY NOT BE ADEQUATELY DESCRIBED IF THE CLAIMS REQUIRE AN ESSENTIAL OR CRITICAL ELEMENT WHICH IS NOT ADEQUATELY DESCRIBED IN THE SPECIFICATION AND WHICH IS NOT CONVENTIONAL IN THE ART" (Column 3, page 71434), "WHEN THERE IS SUBSTANTIAL VARIATION WITHIN THE GENUS, ONE MUST DESCRIBE A SUFFICIENT VARIETY OF SPECIES TO REFLECT THE VARIATION WITHIN THE GENUS", "IN AN UNPREDICTABLE ART, ADEQUATE WRITTEN DESCRIPTION OF A GENUS WHICH EMBRACES WIDELY VARIANT SPECIES CANNOT BE ACHIEVED BY DISCLOSING ONLY ONE SPECIES WITHIN THE GENUS" (Column 2, page 71436).

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states that "APPLICANT MUST CONVEY WITH REASONABLE CLARITY TO THOSE SKILLED IN THE ART THAT, AS OF THE FILING DATE SOUGHT, HE OR SHE WAS IN POSSESSION *OF THE INVENTION.* THE INVENTION IS, FOR PURPOSES OF

THE 'WRITTEN DESCRIPTION' INQUIRY, *WHATEVER IS NOW CLAIMED.*" (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at page 1116).

One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481, 1483. In *Fiddes*, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence.

In view of these considerations, a skilled artisan would not have viewed the teachings of the specification as sufficient to show that the applicant was in possession of the claimed invention commensurate to its scope because it does not provide adequate written description for the broad class of or representative species of ligand-binding regions that can bind to a FK506 and/or FK506 analog. Therefore, only the described FK506-binding protein (FKBP) meets the written description provision of 35 U.S.C. §112, first paragraph.

To the extent that the claimed methods are not described in the instant disclosure, claims 25, 27-33, 41, 43, 44, 46-53, 56-71, 74-91, 94, 95 are also rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention, since a disclosure cannot teach one to make or use something that has not been described, and was not conventional in the art.

Claims 25, 27-29, 32, 33, 41, 43, 44, 46-48, 51-84, 87-95 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for activating an antigen-presenting cell comprising transfecting an antigen presenting cell *ex vivo* with an expression vector, or *in vivo* in a subject by propelling particles containing the expression vector, wherein the expression vector comprises a polynucleotide encoding a chimeric protein comprising a myristoylation membrane targeting region, a ligand-binding region that is a FK506-binding protein, a CD40 cytoplasmic polypeptide region lacking the CD40 extracelluar domain, *wherein the ligand is FK506 or its analogs*; does not reasonably provide enablement for doing so with any non-protein multimeric ligand (e.g. claims 25, 82), any small molecule (e.g. claim 28); and it does not reasonably provide enablement for inducing an immune response *in vitro* (claims 61-75), for reasons of record and following.

Given the broadest reasonable interpretation, instant claims encompass using any non-protein multimeric ligand for binding with FK506. However, the specification fails to teach how these binding pairs would function in the context of the claimed construct expressing a FKBP chimeric protein. The paragraphs 0082 to 0095 of the specification generally name several non-protein drug-ligand binding pairs, such as cyclophilin receptors, the steroid receptors, and tet receptor. However, it fails to teach that these systems are suitable for inducing CD40 receptor dimerization, and it fails to teach how these systems would function a FK506-binding region, and any multimeric ligand in the context of chemically induced dimerization for manipulating CD40 signal

transduction. Given the state of the art as discussed previously, it is incumbent upon applicants to provide sufficient and enabling teachings within the specification for such therapeutic regimen. Although the instant specification provides a list of systems that may be used as non-protein drug binding pairs, it is not enabled for its full scope because the specification fails to provide an enabling disclosure for binding FKBP with any non-protein multimeric ligand.

Claims 61-75 are directed to inducing an immune response, preferably a CTL response *in vitro* in a cultivated population of antigen presenting cells. While the specification teaches *activating APCs* in vitro with an iCD40 system, the specification fails to teach how an immune response could be induced when only APCs are present, and when cytotoxic T lymphocytes do not even present in the culture environment, and not in contact with the CTLs.

Therefore, in view of the limited guidance, the lack of predictability of the art, and the breadth of the claims, one skill in the art could not practice the invention without undue experimentation as it is broadly claimed.

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to **Q. Janice Li** whose telephone number is **571-272-0730**. The examiner can normally be reached on 9:30 am - 7 p.m., Monday through Friday, except every other Wednesday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, **Joseph Woitach** can be reached on **571-272-0739**. The **fax** numbers for the organization where this application or proceeding is assigned are **571-273-8300**.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is **(866) 217-9197**. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

For all other customer support, please call the USPTO Call Center (UCC) at **800-786-9199**.

Q. JANICE LI, M.D.
PRIMARY EXAMINER

Q. Janice Li, M.D.
Primary Examiner
Art Unit 1633

QJL
June 14, 2007